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Original Article

Sleep disorders and circadian rhythm in epilepsy revisited: a prospective controlled study

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ABSTRACT

Objective: Sleep disturbance is reported to be frequent in epilepsy. The role of comorbidity, which is frequently accompanied by sleep disturbance, has not been investigated. The present study assessed sleep disorders and circadian rhythm in patients with epilepsy, in whom relevant comorbidity was carefully excluded.

Methods: Two hundred patients with epilepsy (100 generalized, 100 partial), without relevant psychiatric, neurological or internal comorbidity, were compared with 100 matched controls. The questionnaire contained specifically tailored questions to address the association between epilepsy and sleep disturbance, and validated questionnaires aimed at sleep quality, excessive daytime sleepiness (EDS), circadian rhythm, sleep disorders, and quality of life.

Results: Forty-one percent of the participants reported on the acute effects of present or past seizures on sleep-wake rhythm, whereas chronic effects were not evident. Participants and controls did not differ in the rates of chronic sleep disturbance, EDS, and presence of sleep disorders (all p-values non-significant or n.s.). Apart from earlier sleep times on workdays ($p = 0.001$) in those with epilepsy, circadian variables were similarly distributed. Epilepsy was well controlled, with 75.9% being seizure free for ≥1 year. Longer durations of epilepsy showed a negative correlation with sleep quality (rho = –0.256, $p < 0.001$). Participants with generalized and partial epilepsies did not differ in rates of sleep disturbance, EDS, sleep disorders, and variables of circadian rhythm (all p-values n.s.).

Conclusion: The present study demonstrated that chronic sleep disturbance is not increased in patients with well-controlled epilepsy without relevant comorbidity. This supports comorbidity and insufficient seizure control as major contributors of sleep disturbance in epilepsy.

1. Introduction

Sleep disturbance is a frequently reported complaint in patients with epilepsy [1]. To date, five controlled questionnaire studies with a main focus on sleep disorders, circadian rhythm, and excessive daytime sleepiness (EDS) comprising ≥100 participants with epilepsy have been published [2–6]. The largest of these studies contained data from a mailed questionnaire survey of 486 patients with partial epilepsies. This study demonstrated that the rate of sleep disturbance was twice as high as in the controls [4]. In addition, those with epilepsy and sleep disturbance had a worse quality of life than those without sleep disturbance [4]. A three-time increased rate of sleep disturbance was reported in a more heterogeneous sample of 100 patients with both partial and generalized epilepsies [5]. Concerning circadian rhythm, people with epilepsy have been shown to be more morning-oriented, with earlier mid-sleep, and have longer sleep duration on non-work days compared with a population-based control sample [6]. Two other studies have looked at possible factors related to subjective daytime sleepiness in epilepsy [2,3]. Both authors showed that symptoms suggestive of obstructive sleep apnea are independent predictors of subjective daytime sleepiness in epilepsy [2,3]. In addition, seizure frequency was found to be an epilepsy-intrinsic contributor to daytime sleepiness [3].

The influence of associated comorbidities on the presence of sleep disturbance or EDS has not been addressed in these studies [2–6]. Of note, mood or anxiety disorders are frequent in patients with epilepsy, and can affect up to 39% of subjects [7]. Mood and anxiety disorders, however, are often associated with increased rates of sleep disturbance [8,9]. It can therefore be speculated that it is not epilepsy itself, but its associated comorbidities, that contribute to the increased rate of sleep disturbance in epilepsy. In addition, none of the previous studies have been adequately powered to compare between patients with partial and generalized epilepsies [2,3,5,6].

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In this light, the present study aimed to investigate sleep disorders and circadian rhythm in both partial and generalized epilepsies compared with healthy controls, in an adequately powered sample size after exclusion of psychiatric, neurological or internal comorbidities. This question is of great relevance to understanding the role of epilepsy itself in chronic sleep disturbance in patients with epilepsy.

2. Design and methods

2.1. Study population

A total of 100 consecutive patients with idiopathic, generalized epilepsy, and 100 consecutive patients with partial epilepsy were recruited at the outpatient epilepsy clinic of Medical University of Innsbruck between November 2012 and November 2013. Inclusion criteria were: the presence of either unequivocal, generalized or partial epilepsy, based on clinico-electrographic characteristics as well as magnetic resonance imaging (MRI); being aged between 18 and 80 years at the time of investigation; and an onset of epilepsy prior to 60 years of age. Major exclusion criteria were: shiftwork; a Mini Mental State Examination score below 26 [10]; documented or suspected non-epileptic seizures; and psychiatric, neurological or relevant internal comorbidity. Psychiatric comorbidity was based on the patient's history, a score above 10 in the Hospital Anxiety and Depression Scale [11], information gathered from the treating physician, and a review of the electronic hospital management information system. Both groups of patients with epilepsy were compared with 100 gender- and age-matched (+/– 2.5 years) healthy controls. These controls were recruited from either non-related acquaintances of patients, or hospital staff and their acquaintances or family members. The exclusion criteria for the controls corresponded to those of the patients with epilepsy, except that central nervous system active medication was a further exclusion criterion for the healthy controls.

Ethical committee approval was obtained at Medical University of Innsbruck. All patients granted written informed consent according to the Declaration of Helsinki.

2.2. Applied questionnaire

All study participants underwent a comprehensive structured sleep questionnaire, which consisted of a face-to-face semi-structured interview (Part 1) and self-administered validated scales (Part 2). The scales were distributed to all participants after giving them a short explanation on how to fill in the scales. Ambiguous answers were discussed. The completed questionnaires were re-checked for consistency or missing values. Demographic and clinical information were gathered from the participants' file notes.

The questionnaire consisted of questions specifically tailored to address the association between epilepsy and sleep disorders and sleep hygiene, as well as validated scales aimed at sleep quality (Pittsburgh sleep quality index) [12], EDS (Epworth sleepiness scale) [13], suspected sleep-related breathing disorders (Berlin questionnaire) [14], circadian rhythm (Munich chronotype questionnaire) [15], movement disorders during sleep, parasomnias and isolated findings (Munich parasomnia scale [16], Innsbruck REM sleep behavior disorder or RBD inventory [17], and quality of life or QOLIE-31 [18,19].

2.2.1. Pittsburgh sleep quality index

The Pittsburgh sleep quality index is composed of seven subscores aimed at subjective sleep quality, sleep latency, sleep duration, sleep efficiency, sleep disturbances, use of hypnotics, and daytime sleepiness. The maximum total score is 21 points. A score of 10 points and higher is indicative for the presence of chronic sleep disturbance [12].

2.2.2. Epworth sleepiness scale

The Epworth sleepiness scale assesses daytime sleepiness in eight different everyday-life situations. Each situation has to be rated from 0 to 4; the maximum score is 24. A cut-off of 10 and higher is accepted to indicate EDS [13].

2.2.3. Berlin questionnaire

This questionnaire screens for obstructive sleep apnea syndrome. It comprises three categories (Category 1 consists of five questions assessing snoring; Category 2 consists of four questions assessing EDS; Category 3 consists of one question asking for arterial hypertension). The Berlin questionnaire is rated to be positive when two of the three symptom categories are answered positively [14].

2.2.4. Munich chronotype questionnaire

This is a chronotype questionnaire that separately assesses sleep–wake pattern on working days and non-working days [15]. Reported outcome variables are the time of midsleep (midtime between sleep onset and sleep end), social jetlag (difference between the time of midsleep on workdays and the time of midsleep on non-working days), and accumulated sleep deprivation (difference between the average sleep duration and the sleep duration on work days, taking into account the number of work days/week).

2.2.5. Munich parasomnia scale

The Munich parasomnia scale is a self-rating instrument with 21 items assessing the lifetime prevalence and current frequency of parasomnias and nocturnal behaviors in adults. For the individual items, the sensitivity is equal to or greater than 90% for all but two of the 21 items, and specificity is above 80% for all items and above 90% for 19 of the 21 items [16].

2.2.6. Innsbruck REM sleep behavior disorder inventory

The Innsbruck RBD inventory is a five-item screening questionnaire for RBD. A cut-off of 0.25 is shown to be suggestive for potential RBD [17].

2.2.7. QOLIE-31

The QOLIE-31 is a 31-item quality of life questionnaire comprising seven subscales covering general and epilepsy-specific domains. Its subscales are grouped into two factors: emotional/psychological effects and medical/social effects. The present study calculated the total score as well as all seven subscores. The maximum total score is 100. A higher total score is associated with a better quality of life [18,19].

2.3. Sample size estimation and statistical analysis

The sample size was estimated with 100 subjects per group, based on the assumption of a significance level of 0.05, a power of 0.95, and a reported three-times increased frequency of sleep disturbance in patients with epilepsy compared with controls [5]. Normality distribution was assessed with the Kolmogorov–Smirnov Test. In case of normal distribution, means +\– standard deviations were given; in case of abnormal distribution, medians and ranges were given. Group comparisons were performed with independent *t*-tests in case of normal distribution, or the Mann–Whitney *U*-test or Kruskal–Wallis test in case of abnormal distribution. Categorical variables were compared with the Chi-squared test (Pearson test or two-sided Fisher's exact test, as applicable). Bonferroni correction was applied in order to correct for multiple comparisons, and the level of significance was set accordingly. Further, to account for the intake of antiepileptic medication, binary logistic analysis was performed; sex, age, and intake of antiepileptic medication were entered as covariates. To

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Table 1
Demographic characteristics of the study population.

	Participants with epilepsy (200)	Controls (100)	*p*-Value
Sex, *n* women (%)	103 (51.5)	46 (46.0)	0.369
Age, y (median, range)	35 (18.0–74.0)	33.5 (18.0–74.0)	0.998
Age at epilepsy onset (median, range)	17.0 (0.0–59.0)		
Duration of epilepsy[a] (median, range)	9.0 (0.0–57.0)		
Body mass index (median, range)	23.5 (16.0–49.0)	23.6 (17.0–45.0)	0.827
Current bed partner, *n* (%)	144 (72.0)	77 (77.0)	0.644

[a] Duration of epilepsy was calculated from the first year to the last year of seizures.

assess the predictors of EDS in patients with epilepsy, a logistic regression analysis adjusted for sex and age, using the Wald backward procedure, was applied. All statistical analyses were performed with IBM SPSS version 22 for Windows.

3. Results

3.1. Demographic and clinical characteristics of the study participants

The participants were 200 adults with epilepsy, with a median age of 35 years (range 18–74) and a median age at epilepsy onset of 17 years (range 0–59). Participants were compared with 100 gender- and age-matched controls. Table 1 summarizes the demographic characteristics of the study population.

One hundred participants had idiopathic generalized epilepsies and 100 had partial epilepsies. Sixty-eight percent of partial epilepsies were lesional epilepsies. Eighteen percent of participants with partial epilepsies reported having exclusive sleep-related seizures. One hundred and eighty-one participants of the total sample (90.5%) were under current antiepileptic medication (70% monotherapy and 30% polytherapy). The four most commonly used drugs were: levetiracetam (69 participants), valproic acid (58 participants), lamotrigine (33 participants), and controlled-release carbamazepine (30 participants). Thirty-five of the 100 participants with partial epilepsies (35%) had previously undergone surgery for epilepsy. Epilepsy was well controlled in the majority of cases: overall, 94.9% reported their epilepsy to be stable or improved over the last six months, whereas 5.1% indicated their epilepsy to have worsened. Moreover, during the last year, 75.9% of all participants were seizure free. The distribution of epilepsy syndromes, seizure types, and seizure frequency are provided in Table 2. The median QOLIE-31 score was 83.2 (range 32.1–100).

3.2. Sleep disorders and circadian rhythm in epilepsy vs controls

Forty-one percent of the participants with epilepsy (82/200) reported acute effects of present or past epileptic seizures on the sleep–wake rhythm: 82 (41.0%) indicated that nocturnal seizures resulted in increased sleepiness on the following day, 32 (16.0%) reported on the necessity of an immediate nap following a diurnal generalized seizure, and 10 (5.0%) complained of disturbed nocturnal sleep after diurnal generalized seizures. In contrast to these direct influences of seizures on nocturnal sleep and daytime sleepiness, rates of chronic sleep disturbance and EDS did not differ between patients with epilepsy and controls. Chronic sleep disturbance was reported in 1.5% of participants with epilepsy compared with 3.0% of the healthy controls ($p = 0.405$); EDS was reported in 8.0% of the participants with epilepsy compared with 14.0% in the controls ($p = 0.106$). Lifetime prevalence of all sleep disorders, as assessed with the Munich parasomnia scale and the Innsbruck RBD inventory, did not differ between both groups. Information on various sleep disorders and their distribution among participants and controls is provided in Table S1 of the Appendix: Supplementary material. Adjustment for the intake of antiepileptic medication did not change any of these results (see corrected *p*-values in Table S2 of the Appendix: Supplementary material). There was a negative correlation between the duration of epilepsy and sleep quality, as assessed with the Pittsburgh Sleep Quality Index (Spearman rho = –0.256, $p < 0.001$).

Table 3 shows the results of the Munich chronotype questionnaire assessing the circadian rhythm on workdays and non-workdays in participants and controls: participants with epilepsy reported earlier sleep onset times on workdays ($p = 0.001$). Sleep onset times on non-workdays, midsleep and sleep-end on work days and non-workdays, as well as total sleep duration, social jetlag, and accumulated sleep deprivation, did not differ between both groups after correction for Bonferroni. Adjustment for the intake of antiepileptic medication led to similar results, except that sleep onset times on workdays did no longer withstand correction for Bonferroni (data not shown). Moreover, participants with epilepsy more carefully respected regular sleep times than controls (86.4% of epilepsy vs 78.0% of controls, $p = 0.043$).

3.3. Sleep disorders and circadian rhythm in participants with generalized vs partial epilepsies

Rates of chronic sleep disturbance, EDS, and the lifetime prevalence of sleep disorders did not differ between participants with

Table 2
Epilepsy syndrome, seizure type and seizure frequency of the population sample.

	Participants with epilepsy (200)
Epilepsy syndrome	
Generalized, *n* (%)	100 (50)
CAE, % generalized	10
JAE, % generalized	22
JME, % generalized	28
GMA, % generalized	40
Partial, *n* (%)	100 (50)
TLE, % partial	82
FLE, % partial	17
OLE, % partial	1
Seizure type	
Focal seizures, *n* (%)	100 (50)
Without impairment of consciousness or awareness, %	70
With impairment of consciousness or awareness, %	58
Evolving to a bilateral convulsive seizure, %	74
Generalized seizures, *n* (%)	100 (50)
Absence, %	41
Myoclonic, %	33
Tonic-clonic, %	100
Seizure frequency	
Seizure free >1 year, %	75.9
0 in last 6 months, %	81.8
<5 in last 6 months, %	13.6
1–2 per month, %	2.5
> 1 per week, %	2

CAE, childhood absence epilepsy; FLE, frontal lobe epilepsy; GMA, generalized epilepsy with GM on awakening seizures; JAE, juvenile absence epilepsy; JME, juvenile myoclonic epilepsy; OLE, occipital lobe epilepsy; TLE, temporal lobe epilepsy.

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Table 3
Circadian rhythm in participants with epilepsy and controls.

Circadian variables	Participants with epilepsy (200)	Controls (100)	*p*-Value	Generalized epilepsy (100)	Partial epilepsy (100)	*p*-Value
Sleep onset on workdays	22:35 (20:06–03:00)	23:10 (21:00–04:01)	0.001*	22:40 (20:06–01:15)	22:33 (20:30–03:00)	0.213
Midsleep on workdays	02:30 (23:15–06:30)	02:45 (00:45-08:06)	0.022	02:35 (00:48–06:15)	02:30 (23:15–06:30)	0.108
Sleep end on workdays	06:15 (02:00–12:00)	06:15 (04:00–12:00)	0.341	06:25 (04:00–12:00)	06:00 (02:00–10:30)	0.178
Sleep duration on workdays, h	7.6 (4.8–11.5)	7.5 (4.5–10.4)	0.314	7.5 (5.3–11.5)	7.7 (4.8–10.8)	0.777
Sleep onset on non-workdays	23:30 (20:00–3:10)	00:05 (21:00–04:25)	0.008	23:31 (20:35–03:10)	23:20 (21:15–03:00)	0.810
Midsleep on non-workdays	03:45 (23:30–08:20)	04:10 (01:00–08:43)	0.103	03:56 (01:18–08:20)	03:38 (01:35–07:47)	0.233
Sleep end on non-workdays	08:00 (04:30–13:30)	08:00 (05:00–13:00)	0.457	08:00 (05:00–13:30)	07:30 (04:30–13:00)	0.046
Sleep duration on non-workdays, h	8.6 (4.8–12.9)	8.4 (4.8–13.5)	0.235	8.8 (5.3–12.9)	8.3 (4.8–11.8)	0.012
Social jetlag, h	1.1 (0.0–5.6)	1.0 (0.0–5.6)	0.956	1.2 (0.0–5.6)	1.0 (0.0–4.1)	0.432
Accumulated sleep deprivation, h	1.1 (0.0–6.9)	1.1 (0.0–7.6)	0.892	1.4 (0.0–6.4)	0.7 (0.0–6.7)	0.121

Data are present as median (range).
* Significant *p*-values withstanding correction for Bonferroni.

generalized vs partial epilepsy syndromes. Reported chronic sleep disturbance was present in 1.0% of participants with generalized epilepsies compared with 2.0% with partial epilepsies ($p = 1.000$); EDS was reported in 11.0% of the participants with partial epilepsies compared with 5.0% of those with generalized epilepsies ($p = 0.113$). Rates of sleep disorders are given in Table S1 of the Appendix: Supplementary material. Adjustment for the intake of antiepileptic medication did not change any of these results (see corrected *p*-values in Table S2 of the Appendix: Supplementary material).

Table 3 provides the results on circadian rhythm in participants with generalized vs partial epilepsy syndromes. None of the investigated variables withstood correction for Bonferroni. Adjustment for the intake of antiepileptic medication did not change any of these results (data not shown). As expected, sleep deprivation was a more commonly reported trigger factor for seizures in the generalized epilepsy group (generalized vs partial epilepsy: 45.0% vs 24.0%, $p = 0.002$). Circadian rhythm was similar across the different subtypes of generalized epilepsies (childhood and juvenile absence epilepsy, juvenile myoclonic epilepsy, generalized epilepsy with awakening grand mal seizures) (all *p*-values n.s.).

3.4. Differences in the rate of sleep disorders and circadian rhythm between seizure-free and non-seizure-free patients

Not unexpectedly, seizure-free patients reported less EDS than non-seizure-free patients (seizure-free vs non-seizure-free: 5.3% vs 16.7%, $p = 0.012$). Adjustment for the intake of antiepileptic medication did not change this result ($p = 0.008$). The rates of chronic sleep disturbance, as well as reported sleep disorders and the assessed variables of circadian rhythm, did not differ between both groups (data not shown).

3.5. Predictors of excessive daytime sleepiness in epilepsy

EDS was reported by 8.0% of the patients with epilepsy. Patients with and without EDS differed in the seizure rate during the last six months, drug resistance (defined as failure of adequate trials of two tolerated and appropriately chosen and used antiepileptic drugs to achieve sustained seizure freedom), seizure deterioration over the last six months, and suspected sleep apnea. Type of epilepsy, use of antiepileptic medication, sleep quality, the accumulated weekly sleep deficit, as well as sex, age and BMI were not different between participants with and without EDS (for further information see Table 4). When entering all variables, which were significant in the univariate analysis, in a sex- and age-adjusted linear regression model, only drug resistance (OR 3.2, 95% CI 1.0 to 9.5) and suspected sleep apnea (OR 7.2, 95% CI 1.1 to 45.6) remained significant, independent predictors of EDS in epilepsy.

4. Discussion

The present study is the first case-control investigation of sleep disorders and circadian rhythm in patients with epilepsy in whom relevant neurologic, psychiatric or internal comorbidities were carefully excluded. In addition, it is the first adequately powered head-to-head comparison of the frequency of sleep disorders and circadian rhythm in patients with generalized vs partial epilepsies.

The main findings were that seizures had acute effects on sleep–wake rhythm, whereas chronic sleep disorders were not more common in patients with epilepsy, compared with healthy controls. In line with this finding, no difference in the rate of sleep disorders was observed between patients with generalized onset and partial onset epilepsies. Furthermore, the circadian rhythm, as expressed by the time of midsleep, did not differ between patients with generalized and partial epilepsies, as well as healthy controls.

Table 4
Analysis of patients with epilepsy, with and without excessive daytime sleepiness.

Variables	Patients with epilepsy and EDS ($n = 16$)	Patients with epilepsy without EDS ($n = 184$)	*p*-value
General variables			
Body mass index	24.4 (20.0–32.0)	23.5 (16.0–49.0)	0.476
Age	35 (23–62)	35 (18–74)	0.376
Sex, men %	62.5	47.0	0.234
Epilepsy-specific variables			
Epilepsy onset, age	19 (3–51)	17 (0–59)	0.396
Epilepsy type, focal %	69.0	48.1	0.113
Seizure rate			0.017
0 seizures/6 months, %	56.3	83.1	
< 1 seizure/month, %	37.5	12.0	
≥ 1 seizure/month, %	6.3	4.9	
Drug resistance[a], %	43.8	19.1	0.021
Seizure aggravation over the last 6 months, %	25.0	3.3	0.001
Medication			0.100
No therapy, %	6.3	9.3	
Monotherapy, %	43.8	65.6	
Combination therapy, %	50.0	25.1	
Sleep specific variables			
Pittsburgh Sleep Quality Index	4.5 (1–10)	4 (0–10)	0.190
Accumulated sleep deprivation, h	1.2 (0–3.6)	1.1 (0–6.9)	0.630
Suspected sleep apnea, %	12.5	2.2	0.021

[a] Drug resistance was defined as failure of adequate trials of two tolerated and appropriately chosen and used antiepileptic drugs to achieve sustained seizure freedom.

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Up to 41% of the participants in the study reported on the acute effects of present or past seizures on the sleep–wake rhythm (ie, increased daytime sleepiness after nocturnal seizures, the necessity of an immediate nap after a diurnal generalized seizure and disturbed nocturnal sleep after diurnal generalized seizures). In contrast, the presence of chronic sleep disturbance or increased rates of sleep disorders were not evident. This latter finding challenges the existing literature [2–6] but is likely explained by major differences in the investigated participant samples. Whereas previous studies did not exclude or address the contribution of comorbidities to sleep disturbance in epilepsy [2–5], the present study was specifically designed to investigate the intrinsic role of epilepsy by carefully excluding relevant comorbidities as confounding factors. Of note, psychiatric disorders, which are known to occur in up to 39% of patients with epilepsy [7] and are frequently associated with sleep disturbances themselves [8], could be responsible for the increased rates of sleep disturbance in epilepsy reported in the literature [2–6].

Seizure rate has been assumed to present an important contributor to chronic sleep disturbance in epilepsy. This speculation can only be indirectly answered by the present study. Because the vast majority of participants with epilepsy reported their disease to be stable or improved, and nearly 80% were seizure free for at least one year, it could be hypothesized that the absence of increased sleep disturbance might correspond, at least in part, to the well-controlled status of the disease. In contrast, whether the demonstrated acute effects of seizures could result in chronic sleep disturbance in more severely affected patients is tempting to speculate. The duration of epilepsy in the present study showed a negative correlation with sleep quality – although the general disease course was rather well controlled. In line with this finding, earlier studies of patients with drug-resistant epilepsy have demonstrated that the rates of sleep disorders are more pronounced in this patient subgroup [20].

Antiepileptic drugs were shown to result in increased daytime sleepiness or somnolence, as well as sleep disruption, with first-generation drugs having more pronounced side effects than second-generation medication [21]. In this context, it is interesting to point out that although the majority of participants with epilepsy in the present study were on antiepileptic drug treatment, with both first- (valproic acid, carbamazepine) and second-generation medication (levetiracetam, lamotrigine), EDS or nocturnal sleep complaints were not increased in patients with epilepsy compared with healthy controls. Moreover, adjustment for the intake of antiepileptic medication did not change the abovementioned results, although the group of patients without antiepileptic medication was too small to draw any final conclusions. Furthermore, it might be speculated that good seizure control might even be protective against sleep and wake disturbances, as shown for this patient sample. Indeed, seizure-free patients reported less-frequent excessive daytime sleepiness than those with ongoing seizures.

The present study performed a direct comparison between patients with generalized and partial epilepsies following statistical power considerations. Up to now, idiopathic epilepsies were either investigated in comparatively small population samples [22] or presented a subgroup of patients with epilepsy investigated for sleep disorders [2,3,5,6]. In line with the present results for epilepsy in general, it was found that rates of chronic sleep disorders did not differ between generalized and partial epilepsies. In contrast, seizure-precipitating factors such as sleep deprivation or disturbed nocturnal sleep were, as expected, more frequently present in patients with idiopathic generalized than partial epilepsy.

REM sleep behavior disorder has been suggested to be more common, with 12.5% in patients with epilepsy older than 60 years [23] than in the general population [24–26]. In the present study, we investigated whether the rate of potential RBD, as assessed with the Innsbruck RBD inventory [17], would also be increased in younger patients with epilepsy and whether there is a difference between idiopathic and partial epilepsy cases. No increased rates were found for potential RBD in patients with epilepsy, compared with healthy controls, as well as between idiopathic generalized and partial onset epilepsy cases. Based on this result, it might be suggested that RBD is not an intrinsic trait of epilepsy itself, but can evolve with advancing age, either due to chance co-occurrence, as RBD is more common in the elderly, or be based on a common underlying neurodegenerative process, in the case of symptomatic late-onset epilepsy.

Of note, the circadian rhythm, as expressed by the time of midsleep, did not differ between patients with epilepsy and healthy controls. The same was true for a comparison between patients with generalized versus partial onset epilepsies. The only significant differences in all investigated variables addressing the circadian rhythm were that patients with epilepsy had earlier sleep times on workdays than the controls. Hofstra et al. drew a similar conclusion: they found that patients with juvenile myoclonic epilepsy, temporal lobe epilepsy, and frontal lobe epilepsy exhibited a comparable circadian rhythm [6]. In contrast, Pung and Schmitz, who used the Horne Östberg questionnaire [27], showed a delay in the circadian chronotype in 20 patients with juvenile myoclonic epilepsy [22].

Eight percent of the patients with epilepsy had an Epworth sleepiness score ≥10, which is suggestive of EDS. Admitting that the sample size available for this analysis was small, it was found that EDS in epilepsy was predicted by therapy refractoriness and suspected sleep apnea. The finding of suspected sleep apnea as a major contributor of EDS in epilepsy is well in line with the literature [2,3]. So far, the contribution of seizure rate has been controversially discussed: whereas Malow found no contribution of seizure rate on presence of EDS [2], Manni et al. demonstrated that EDS was primarily due to suspected sleep apnea as well as present seizure rate [3].

In the present, comparatively well-controlled epilepsy population with no increased rates of sleep disturbance, the reported quality of life outcome scores were found to be high, with a median of 83 points on the QOLIE-31 [18,19]. This finding probably reflects a large questionnaire study in 247 adults addressing the relative contributions to quality of life scores in patients with epilepsy. The authors demonstrated that sleep disturbance has a major impact on quality of life [28].

Data on frequencies of sleep disorders are gathered from self-administered validated questionnaires, which are useful instruments for providing frequency estimations, but are subjective in nature and do not substitute face-to-face expert interviews or video-polysomnography, the gold standard in the objective assessment of sleep disorders. In addition, due to the strict inclusion and exclusion criteria, the investigated sample of patients with epilepsy is comparatively selective and does not reflect the general population of patients with epilepsy. Moreover, the rate of seizure-free patients was high. This probably further contributed to the low frequency of sleep disorders, as observed in the present study.

In summary, this large, case-control questionnaire study revealed that seizures do have an impact on acute sleep disturbances, whereas chronic sleep disorders are not more commonly reported in patients with well-controlled epilepsy without relevant comorbidity than in healthy controls. This supports the notion that it is not epilepsy *per se*, but insufficient seizure control, as well as comorbidity that are the main contributors to sleep disorders in epilepsy in general. Future studies using video-polysomnography to objectify the current findings are warranted.

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Conflict of interest

None declared.

The ICMJE Uniform Disclosure Form for Potential Conflicts of Interest associated with this article can be viewed by clicking on the following link: http://dx.doi.org/10.1016/j.sleep.2014.09.021.

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Appendix: Supplementary material

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